AR201-14079

Karen Hoffman

11/19/2002 03:17 PM

To: Barbara Leczynski/DC/USEPA/US@EPA, NCIC HPV@EPA, Jodi Burgess/DC/USEPA/US@EPA
cc:
Subject: HPV Submission on Hexanedioic acid, Di-C7-C9, branched and linear alkyl ester

----- Forwarded by Karen Hoffman/DC/USEPA/US on 11/19/02 03:15 PM -----

"Johannsen, Frederick R" <frjoha@solutia.com> on 11/19/2002 01:21:03 PM

To: Rtk Chem/DC/USEPA/US@EPA
cc: "Mieure, James P" <jpmieu@solutia.com>
Subject: HPV Submission on Hexanedioic acid, Di-C7-C9, branched and linear alkyl ester

Please receive the following attachments containing our submission letter, a Test Plan and Robust Summaries for the aforementioned chemical.

FR Johannsen

<<HPV97Adipatetrans.doc>> <<HPV - 97 ADIPATE.doc>>
<<97adipate.rtf>>

- HPV97Adipatetrans.doc
- HPV - 97 ADIPATE.doc
- 97adipate.rtf

Solutia Inc.
575 Maryville Centre Drive
St. Louis, MO 63141

P.O. Box 66760
St. Louis, MO 63166-6760

November 19, 2002

Christine Todd Whitman, Administrator
U.S. Environmental Protection Agency
P.O. Box 1473
Merrifield, VA 22116

Attn: Chemical Right-to-Know Program
In re: HPV Challenge Program
AR-201

Hexanedioic acid, Di-C7-C9 Branched and Linear Alkyl Ester
CAS Number 68515-75-3

Solutia, Inc., Company Registration Number , is pleased to submit the attached Test Plan and Robust Summaries for the chemical Hexanedioic acid, Di-C7-C9 Branched and Linear Alkyl Ester (CAS No. 68515-75-3) as a part of our commitment to the EPA High Production Volume Challenge Program (AR-201).

The attached files are:

1. This cover letter in MS Word 2000
2. Category Test Plan in MS Word 2000
3. Robust Summaries (IUCLID format) in MS Word 2000

The complete matrix of SIDS data elements, including physical/chemical properties and results of biological and toxicology studies, indicate that no additional testing is required. Please contact me at 314-674-8815 if there are any questions relating to this submission.

Sincerely,

Frederick R. Johannsen

HIGH PRODUCTION VOLUME (HPV)

CHEMICALS CHALLENGE PROGRAM

TEST PLAN

For

HEXANEDIOIC ACID, DI-C7-C9 BRANCHED AND LINEAR ALKYL ESTER (97 ADIPATE)

CAS NO. 68515-75-3

Prepared by:

Solutia Inc. Registration No.

575 Maryville Centre Drive,
St. Louis, Missouri 63141

EXECUTIVE SUMMARY

Solutia Inc. voluntarily submits the following screening information data and Test Plan covering the chemical, Hexanedioic acid, Di C7-C9 branched and linear alkyl ester or 97 Adipate (CAS No. 68515-75-3), for review under the Environmental Protection Agency's High Production Volume (HPV) Chemicals Challenge Program.

A substantial amount of data exists to evaluate the potential hazards associated with 97 Adipate. Use of key studies available from data already developed provide adequate support to characterize each Endpoint in the HPV Chemicals Challenge Program without the need for additional unnecessary testing.

TABLE OF CONTENTS

TEST PLAN FOR 97 ADIPATE

I. INTRODUCTION AND IDENTIFICATION OF CHEMICAL

Under EPA's High Production Volume (HPV) Chemicals Challenge Program, Solutia Inc. has committed to voluntarily compile basic screening data on Hexanedioic acid, Di-C7-C9 Branched and Linear Alkyl Ester, also known as 97 Adipate. The data included in this Test Plan involve physicochemical properties, environmental fate, and human and environmental effects of 97 Adipate, as defined by the Organization for Economic Cooperation and Development (OECD). The information provided comes from existing data developed on behalf of Solutia Inc. or found in the published scientific literature or from estimation modeling and fulfills Solutia's obligation to the HPV Challenge Program.

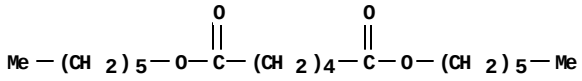
A. Structure and Nomenclature

Following is a characterization of 97 Adipate and associated nomenclature.

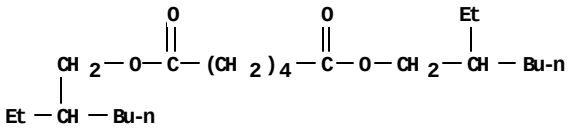
97 Adipate is classified as a UVCB chemical (i.e. a Chemical Substance of Unknown or Variable Composition, Complex Reaction Products and Biological Materials) on the TSCA Chemical Substance Inventory (US EPA, 1985). As such, it does not have a defined structure to depict here. Following is the appropriate nomenclature to reference 97 Adipate:

Hexanedioic acid, di-C7-9-branched and linear alkyl esters
CAS No. 68515-75-3
Synonyms: 97 Adipate, Dialkyl Adipate, Santicizer 97, Santicizer 97A

Two additional adipic acid esters, both closely related structurally to 97 Adipate, have been used to provide surrogate data for the Mutagenicity – Chromosomal Aberration Endpoint, as described in Section IV.D.3.0 of this Dossier. Following are their structures:



Di(n-Hexyl) Adipate
CAS No. 110-33-8
Synonyms: DHA; Santicizer 367; XA-2562 Plasticizer



Dioctyl Adipate
CAS No. 103-23-1
Synonyms: DOA; Di(2-ethylhexyl)adipate; DEHA

B. Manufacturing and Use

97 Adipate is a plasticizer formed by reacting adipic acid with a mixture of lightly branched heptyl and nonyl alcohols. It is specifically designed to give PVC film, sheet and coatings excellent low-temperature flexibility. End products which might contain this plasticizer include coated fabrics or sheeting for rainwear, film for luggage and accessories, and coated industrial fabrics exposed to refrigeration. It is used to plasticize rubber formulations. It imparts good low temperature flexibility to nitrile rubber without reducing its heat aging performance.

It is also used in food packaging, especially for foods which need to be refrigerated or frozen. 97 Adipate complies with US Department of Agriculture regulations for use as an acceptable component of packaging materials in contact with meat or poultry food products prepared under Federal inspection. It is also used in certain indirect food contact applications regulated under sections 175, 176, 177 and 178 of Title 21, Code of Federal Regulations.

97 Adipate is manufactured at one plant in Canada and is imported by Solutia Inc. into the United States. The manufacturing process is a closed process and follows typical Good Manufacturing Practices.

II. TEST PLAN RATIONALE

The data obtained and included to support this Test Plan have come from either 1) internal studies conducted by/or for Solutia Inc. (or its predecessor Monsanto Co.), 2) have been extracted from the scientific literature either as primary references or as found in well-accepted, peer-reviewed reference books, 3) were estimated using environmental models accepted by the US EPA (1999b), or 4) were associated with structurally similar adipate esters and thus found useful to provide a “read across” assessment of a single (Chromosomal Aberration) HPV Endpoint.

The basic screening data derived for this initial assessment include information on physicochemical properties, environmental fate, and human and environmental effects associated with 97 Adipate. The data used to support this program include those endpoints identified by the US EPA (1998); key studies for 97 Adipate have been identified for each data Endpoint and are summarized in Robust Summary form and included in Section VI, which accompanies this Dossier. Robust summaries of relevant mutagenicity studies conducted with DHA and DOA, two Adipic acid ester surrogates used in this assessment are also included in Section VI.

All studies were reviewed and assessed for reliability according to standards specified by Klimisch et al (1997), as recommended by US EPA (1999a). The following criteria were used for codification:

1. Reliable without Restrictions – Includes studies which comply with US EPA and/or OECD-accepted testing guidelines, which were conducted using Good Laboratory Practices (GLPs) and for which test parameters are complete and well documented.

2. Reliable with Restrictions – Includes studies which were conducted according to national/international testing guidance and are well documented. May include studies conducted prior to establishment of testing standards or GLPs but meet the test parameters and data documentation of subsequent guidance; also includes studies with test parameters which are well documented and scientifically valid but vary slightly from current testing guidance. Also included were physical-chemical property data obtained from reference handbooks as well as environmental endpoint values obtained from an accepted method of estimation (i.e. EPIWIN).

3. Not Reliable – Includes studies in which there are interferences in either the study design or results that provide scientific uncertainty or where documentation is insufficient.

4. Not Assignable – Not used in this Dossier.

Those studies receiving a Klimisch rating of 1 or 2 are considered adequate to support data assessment needs in this Dossier.

III. TEST PLAN SUMMARY AND CONCLUSIONS

Conclusion: All HPV Endpoints have been satisfied with a combination of data from studies that were either well documented, used OECD guideline methods and conducted in accord with GLPs, or were estimated from acceptable estimation

modeling programs. In a single case (Chromosomal Aberration), use of reliable, well conducted studies from two structurally similar surrogate chemicals supports a conclusion that no additional information is needed on 97 Adipate; hence, no further testing is planned, as summarized in Table 1.

In summary:

Physical-chemical property values (Boiling Point, Vapor Pressure, Partition Coefficient and Water Solubility) were obtained from Solutia-derived studies to characterize each of these properties. No Melting Point data is available, or considered applicable, as 97 Adipate is a liquid at room temperature. A rating of "2-Reliable with restrictions" has been assigned to these studies.

Environmental Fate information dealing with Water Stability (Hydrolysis) and Transport (Fugacity) were estimated using a computer estimation-modeling program (EPIWIN, 2002) recommended by EPA (US EPA, 1999b), as no data could be found for either Endpoint. Thus, they have been designated as "2-Reliable with restrictions". Well-conducted and documented studies characterizing Photodegradation and Biodegradation fulfilled each of these Endpoint requirements and have been designated "2-Reliable with restrictions" and "1-Reliable without restriction", respectively.

Each of the three **Ecotoxicity** data (Acute Fish, Acute Invertebrate and Acute Algae Toxicity) Endpoint requirements was met with a respective aquatic toxicity study considered "2-Reliable with restrictions".

Mammalian Toxicity Endpoints for Acute Toxicity and Repeated Dose Toxicity were met with completion of an acute oral rat study and a 13-Week rat toxicity study. As both of these well-documented studies were conducted prior to codification of OECD/GLP guidance, they have been coded "2-Reliable with restrictions"; no effects on the gonads were observed in the 13-Week Subchronic study. Although no study is available addressing Reproductive Toxicity, a Developmental Toxicity study, considered as "1-Reliable without restriction", has been conducted with 97 Adipate. Therefore, according to EPA Guidance (US EPA, 1998a), use of the combination Subchronic study and the Developmental Toxicity study (meeting OECD 414 guidance) will fulfill the HPV Reproductive Toxicity Endpoint. The Ames testing Endpoint is fulfilled with a study classified as "1-Reliable without restriction". No Chromosomal Aberration study has been conducted with 97 Adipate. However, in vivo studies which evaluate the potential to cause chromosomal damage, all of which are considered "1-Reliable without restriction" are available for two adipate esters closely related structurally to 97 Adipate. These studies are deemed adequate for "Read across" evaluation to support this HPV Endpoint for 97 Adipate.

Following is a tabular summary of the Test Plan developed for 97 Adipate.

Table 1. Test Plan Summary for 97Adipate

	Info. Avail.?	OECD?	GLP?	Other Study?	Estimat. Method?	Accept-Able ?	Testing Recomm.?
PHYSICAL CHEMICAL							
Melting Point	N	-	-	-	N	Y	N
Boiling Point	Y	N	N	Y	N	Y	N
Vapor Pressure	Y	N	N	Y	N	Y	N
Partition Coefficient	Y	N	N	Y	N	Y	N
Water Solubility	Y	N	N	Y	N	Y	N
ENVIRONMENTAL FATE ENDPOINTS							
Photodegradation	Y	N	Y	Y	N	Y	N
Stability in Water	Y	-	-	N	Y	Y	N
Biodegradation	Y	Y	N	N	N	Y	N
Transport between Environmental Compartments (Fugacity)	Y	-	-	N	Y	Y	N
ECOTOXICITY							
Acute Toxicity to Fish	Y	N	Y	Y	N	Y	N
Acute Toxicity to Aquatic Invertebrates	Y	N	Y	Y	N	Y	N
Toxicity to Aquatic Plants	Y	N	Y	Y	N	Y	N
MAMMALIAN TOXICITY							
Acute Toxicity	Y	N	N	N	N	Y	N
Repeated Dose Toxicity	Y	N	N	N	N	Y	N
Genetic Toxicity – Mutation (Ames)	Y	Y	Y	N	N	Y	N
Genetic Toxicity – Chromosomal Aberrations	N	-	-	S	N	Y	N
Developmental Toxicity	Y	Y	Y	N	N	Y	N
Reproductive Toxicity	N	-	-	-	N	C	N

Y= Yes; N = No; C = Completed thru combo of Developmental Toxicity and Subchronic Toxicity Endpoints; S = Completed using Surrogate study data; - = Not applicable

IV. DATA SET SUMMARY AND EVALUATION

The key studies used in this assessment to fulfill the HPV requirements have been placed in an Endpoint-specific matrix and further discussed below. Robust Summaries for each study referenced in these tables can be found in Section VI of this Dossier.

A. Chemical/Physical Properties

Table 2. Selected Physical-Chemical Properties of 97 Adipate

Chemical	Boiling Pt. (^{o}C.)	Melting Pt.(^{o} C.)	Vapor Pressure (hPa @ 224 ^{o}C)	Water Solubility (mg/L)	Log Kow
97-Adipate CAS No. 68515-75-3	224	n.a.	13	< 0.048	6.48

n.a. = not applicable; substance is a liquid at room temperature.

All relevant HPV Endpoints for Physical-Chemical Properties have been completed with reliable information taken from well documented studies sufficient to characterize each Endpoint and have been used broadly for that purpose. These studies have been designated as "2-Reliable with restrictions". As 97 Adipate is a liquid at room temperature, there is no melting point value available, nor is one needed.

In summary, 97 Adipate is a liquid with low vapor pressure. It possesses exceedingly low solubility in water and a high Partition coefficient. A calculated bioconcentration factor of >1000 is reflective of its potential to accumulate in biological tissue, unless degradation or metabolism occurs, which is likely, based on comparison to DOA, a structurally similar chemical. The octanol/water Partition coefficient of 97 Adipate and DOA were determined in the same study (Solutia study no. ES-80-SS-41); DOA had a partition coefficient (7.14) and an estimated bioconcentration factor (>2700) even higher than 97 Adipate. Detailed follow up studies with DOA (Felder et al, 1986), confirmed rapid and extensive metabolism and biodegradation occurring in aquatic systems, such that the actual measured bioconcentration factor of DOA (after a 28-d test in bluegills) was 27. A similar rapid and extensive metabolism/biodegradation in the environment would be expected with 97 Adipate.

Conclusion – Adequate studies are available to provide needed information in the physical-chemical properties associated with 97 Adipate. Therefore, no additional data development is needed for these HPV Endpoints.

B. Environmental Fate and Biodegradation

Information obtained from estimation modeling and laboratory testing with 97 Adipate describe the environmental fate and biodegradation characteristics of this chemical, and are highlighted in Table 3. Each of the studies represented in Table 3 are summarized in detail in the Robust Summary section of this Dossier.

Table 3. Environmental Fate and Biodegradation Properties of 97-Adipate

Chemical	Biodegradation Rate (24 hr)	Stability in Water	Fugacity	Photodegradation Rate
97-Adipate CAS No. 68515-75-3	67-88 %	3.21 yrs	Air- 0.3 Water- 3.6 Soil - 27.3 Sed.- 68.8	0 % (14 days)

A well-conducted and documented biodegradation study, which evaluated 97 Adipate for Ready (SCAS Test) and Ultimate Biodegradation (C02 Evolution Test), supports the Biodegradation HPV Endpoint and has been classified as "1-Reliable without restriction". 97 Adipate was also evaluated for Photodegradation potential. Follow up testing was conducted to resolve a question of microbial contamination, which allowed reasoned scientific conclusions to be drawn from this study, which is classified as "2-Reliable with restrictions", to support this Endpoint. Both Fugacity and Stability in Water Endpoints were completed using the EPIWIN (2002) estimation model, as recommended by US EPA (1999b); thus, they have been classified as "2-Reliable with restrictions". The water stability is best estimated for 97 Adipate since it is impossible to conduct the recommended OECD #111 Test with this material. That Test Guideline requires that the test substance be soluble at a level of 20 mM. The calculated water solubility of 97 Adipate is < 48 ppb or 0.13 uMol (based on Mol. Wt. of 356.55 g/Mol), thus rendering the test impractical and any such results analytically meaningless.

In summary, 97 Adipate will partition almost exclusively into the soil/sediment environmental compartment where it is readily biodegradable. While essentially no Photodegradation or hydrolysis can be expected, 97 Adipate is degraded rapidly through bacterial action with no apparent acclimation or induction period apparently being needed to initiate or carry out the process. Limited amounts of 97 Adipate are expected in the aqueous compartment, as it possesses exceedingly low water solubility where it will be degraded via bacterial action.

Conclusion – Adequate studies are available to provide needed information for each of the HPV Environmental Properties associated with 97 Adipate. No additional testing is recommended.

C. Aquatic Toxicity

Each of the three acute aquatic toxicity studies used to support the HPV Aquatic Toxicity Endpoints were well-conducted studies that followed US EPA testing guidance; the methods used were similar to, and subsequently codified, into OECD testing guidance. All studies were conducted in accord with GLPs. Due to the exceedingly low water solubility (< 48 ppb) of 97 Adipate, each study was conducted above this level. In all cases, no interference was observed (i.e. no toxicity observed at the nominal dosage levels used nearest the solubility limit) between test article and test species. Thus, this limitation did not detract from the conclusions reached for an assessment of each study, i.e., 97 Adipate produces no acute toxicity up to levels of aqueous solubility. Based on the limited solubility factor, the results as reported in these studies, and as summarized in Table 4, should be considered in excess of the actual value (i.e. NOEL = 0.048 mg/L) and thus were considered "2-Reliable with restrictions". These studies are, however, fully adequate to fulfill the HPV data requirements for its Endpoint.

Table 4. Aquatic toxicity parameters for 97-Adipate

Chemical	Fish LC 50 (mg/L)	Invertebrate LC50 (mg/L)	Algae EC50 (mg/L)
97-Adipate CAS No. 68515-75-3	>1,000 (96-h trout)	1.9 (48-h daphnia)	2.5 (96-h)

In summary, 97 Adipate produces no overt acute toxicity in any of the three aquatic species tested up to the level of water solubility (< 48 ppb).

Conclusion – Adequate studies are available on fish, aquatic invertebrates and algae in order to assess the acute aquatic toxic hazards associated with 97 Adipate. Therefore, no additional data development is needed for these HPV endpoints.

D. Mammalian Toxicity

Table 5. Summary of Mammalian Toxicity of 97-Adipate

Chemical Name/ CAS no.	Acute Toxicity		Repeat Dose Toxicity.	Developmental Toxicity
	OLD50 (Rat)	DLD50 (Rabbit)	90-Day (Rat oral)	Rat (oral)
97-Adipate CAS No. 68515-75-3	>15,800 mg/kg	> 7,940 mg/kg	NOEL = 2.5 % in diet	NOEL (terata) = 7,000 mg/kg NOEL (embryo/feto) = 4,000 mg/kg NOEL (maternal) = 4,000 mg/kg

1.0 Acute Toxicity

Results of acute toxicity studies by both the oral and dermal routes of exposure have been conducted and Robust Summaries prepared in the Dossier section below. Both studies were conducted prior to inception of OECD and GLP guidelines, but used methodology consistent with OECD testing for the Acute Toxicity Endpoint. The acute oral toxicity study, which is a Minimum Lethal Dose assay, is considered the key study for this HPV Endpoint and fulfills the data needs in this area. The Dermal Minimum Lethal Dose study has been included as Supplemental information. Both studies are considered as "2-Reliable with restrictions".

97 Adipate is considered to be practically non-toxic after acute oral or dermal exposure.

Conclusion – An available acute toxicity study is sufficient to assess the acute hazards associated with 97 Adipate. Therefore, no additional data development is needed for this HPV Endpoint.

2.0 Repeated Dose Toxicity

97 Adipate has been tested in rats by the dietary route for 90 consecutive days (Table 4). A Robust Summary of this study has been included in the appropriate section of this Dossier. As it was conducted consistent with, but prior to, codification of OECD Test guidance (# 408) and GLPs, this study is considered "2-Reliable with restrictions" and is sufficient to meet this HPV Endpoint requirement.

Dietary levels as high as 2.5% (approximately 1500 mg/kg/d for males and 1950 mg/kg/d for females) produced no systemic toxicity. Measurements included body weights, food

consumption, survival, clinical biochemistry and hematology, organ weights and full necropsies and microscopic examination of a full range of tissues. Of note, no effects on reproductive organs (male or female) were observed in this subchronic study.

Conclusion – A 13-Week study by the oral route of exposure has been conducted with 97 Adipate and is sufficient to evaluate the Repeated Dose toxicity for this chemical. Therefore, no additional data development is needed for this HPV Endpoint. Additionally, the lack of effects seen in the male and female reproductive organs allows this study to be used to support the Reproductive Toxicity Endpoint, as discussed below.

3.0 Mutagenicity and Chromosomal Aberrations

Information on one of the two Mutagenicity Endpoints for HPV assessment is available with 97 Adipate. An Ames mutagenicity test, following OECD Test Guideline 471 and conducted according to GLPs, is summarized in Table 6. This study has been designed as "1-Reliable without restriction", is further described in the Robust Summary section of this Dossier, and is sufficient to meet this HPV Endpoint.

No evidence of mutagenic activity was observed in the Ames test with 97 Adipate. Similarly, 97 Adipate elicited no mutagenic activity when tested in a L5178Y TK +/- Mouse Lymphoma assay in mammalian cells (Solutia Study no. SR-80-532-information not summarized in this Dossier).

Thus, it is concluded that adequate testing has been performed on 97 Adipate to evaluate the Ames Test HPV Endpoint.

Table 6. Summary of Mutagenicity Studies with 97 Adipate and Structurally Related Compounds

	Ames Test Results (TA1535, TA1537, TA98, TA100)	Chromosomal Aberration Test Results
97-Adipate CAS No. 68515-75-3	Neg. with and without S9	No Data
Dioctyl Adipate (DOA) CAS No. 103-23-1 [SURROGATE]	Neg. with and without S9	Neg. – Mouse Micronucleus
Di-n-Hexyl Adipate (DHA) CAS No. 110-33-8 [SURROGATE]	Neg. with and without S9	Neg. – Mouse Micronucleus Neg. – *In vivo* Rat bone marrow cytogenetics Neg – *In vitro* Cytogenetics

No tests for evaluation of Chromosomal Aberration potential of 97 Adipate have been located. However, we have identified studies that would fulfill this HPV Endpoint that have been conducted with two structurally similar adipate esters, DOA and DHA. Studies conducted with DOA were selected as DOA is a C8 branched chain adipic acid ester; DHA is a C6 linear chain adipic acid ester (see structures on page 4). 97 Adipate is itself a mixed, branched and linear C7-C9 chain adipic acid ester. Hence, there is sufficient structural similarity and overlap for these two compounds to serve as Surrogates to evaluate the biological potential of 97 Adipate for this Endpoint.

All Chromosomal Aberration Endpoint studies for these chemicals have been summarized in Table 6 below and are further reported in their own, respective sections of the Robust Summary in this Dossier. Each study is considered "1-Reliable without restriction". In order to provide as complete a comparison of the mutagenic potential of all three chemicals as possible, we also have included in Table 6 the results of Ames tests performed with DOA and DHA, along with 97 Adipate. These Ames Tests also have been summarized and included in the Robust Summary section at the end of this Dossier.

Not only is there a close structural similarity between DOA, DHA and 97 Adipate, there is also a consistent **lack of mutagenic activity** seen with all tests performed with these adipic acid esters. Whether evaluated as to potential to cause Chromosomal aberrations via cell culture or in whole animal testing, DOA and DHA were uniformly without mutagenic activity. Similarly, Ames tests with all 5 tester strains (with and without activation) with each of the three adipate esters were uniformly without mutagenic activity. Thus, we believe it is scientifically valid to conclude that 97 Adipate is highly unlikely to cause chromosomal aberrations and that the results of Chromosomal Aberration test results with DOA and DHA can be used as Surrogates to fulfill this HPV Endpoint rather than to conduct a similar study with 97 Adipate.

In summary, use of surrogate Chromosomal Aberration testing with structurally similar adipate esters is sufficient to meet the HPV Endpoint Testing needs for 97 Adipate. Thus, no further, unnecessary testing is planned.

4.0 Reproductive and Developmental Toxicity

An extensive literature search yielded no studies that directly assessed the reproductive toxicity of 97 Adipate. However, a rat Developmental Toxicity study, which was conducted in accord with GLPs and meets OECD Test Guideline 414, is available. It has been summarized in Table 5, and extensively reported in the Robust Summary section of this Dossier. It is considered "1-Reliable without restriction". Results of this study, coupled with the lack of testicular effects observed in the 13-Week rat Repeated Dose study reported above, is sufficient to meet the HPV criteria for the Reproductive Toxicity Endpoint, as outlined by US EPA (1998).

In summary, when tested via gavage at dosages ranging from 1,000 – 7,000 mg/kg/d and administered between gestation days 6-19, 97 Adipate produced maternal (decreased weight and weight gain) toxicity but no evidence of teratogenic effects. A small increase in skeletal variations was observed at 7,000 mg/kg/d, a level which also produced maternal toxicity.

In conclusion, the Reproductive Toxicity HPV Endpoint has been fulfilled with completion of a rat teratology study coupled with the lack of evidence of test article effects on the reproductive organs (male and female) after subchronic (90-day) testing. Thus, no further testing for this Endpoint is warranted.

V. REFERENCES

EPIWIN, 2002. Version 3.10, Syracuse Research Corporation, Syracuse, New York.

Felder, JD, Adams, WJ, Saeger, VW. 1986. Assessment of the safety of Dioctyl Adipate in freshwater environments. Environmental Toxicology and Chemistry 5: 777-784.

Klimisch, H.-J., Andreae, M. and Tillman, U. 1997. A systematic approach for evaluating the quality of experimental toxicological and ecotoxicological data. Regul. Toxicol. Pharmacol. 25:1-5.

US EPA, 1985. Toxic Substances Control Act Chemical Substance Inventory. TSCA Inventory: 1985 Edition. Volume 1. TS-793. EPA-560/7-85-002a. US Environmental Protection Agency, Office of Toxic Substances, Washington, DC.

US EPA, 1998. Guidance for meeting the SIDS requirements (The SIDS Guide). Guidance for the HPV Challenge Program (11/31/98).

US EPA, 1999a. Determining the adequacy of existing data. Guidance for the HPV Challenge Program (2/10/99).

US EPA, 1999b. The use of structure-activity relationships (SAR) in the High Production Volume Chemicals Challenge Program. OPPT, EPA.

VI. ROBUST STUDY SUMMARIES

IUCLID Data Sets, full set for 97 Adipate and selected studies for DOA and DHA, are appended

IUCLID

Data Set

Existing Chemical	:	ID: 68515-75-3
EINECS Name	:	Hexanedioic acid, di-C7-9-branched and linear alkyl esters
Generic name	:	Di(C7-9-alkyl) adipate
CAS No.	:	68515-75-3
EINECS No.	:	271-105-9
Tag name	:	97 Adipate

Producer Related Part

Company	:	Solutia Inc.
Creation date	:	30.04.2001

Substance Related Part

Company	:	Solutia Inc.
Creation date	:	30.04.2001
Memo	:	
Printing date	:	18.11.2002
Revision date	:	30.04.2001
Date of last Update	:	18.11.2002
Number of Pages	:	19
Chapter (profile)	:	Chapter: 1, 2, 3, 4, 5, 7
Reliability (profile)	:	Reliability: without reliability, 1, 2, 3, 4
Flags (profile)	:	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 OECD AND COMPANY INFORMATION

1.0.2 LOCATION OF PRODUCTION SITE

1.0.3 IDENTITY OF RECIPIENTS

1.1 GENERAL SUBSTANCE INFORMATION

1.1.0 DETAILS ON TEM PLATE

1.1.1 SPECTRA

1.2 SYNONYMS

1.3 IMPURITIES

1.4 ADDITIVES

1.5 QUANTITY

1.6.1 LABELLING

1.6.2 CLASSIFICATION

1.7 USE PATTERN

1.7.1 TECHNOLOGY PRODUCTION/USE

1.8 OCCUPATIONAL EXPOSURE LIMIT VALUES

1.9 SOURCE OF EXPOSURE

1.10.1 RECOMMENDATIONS/PRECAUTIONARY MEASURES

1.10.2 EMERGENCY MEASURES

1.11 PACKAGING

1.12 POSSIB. OF RENDERING SUBST. HARMLESS

1.13 STATEMENTS CONCERNING WASTE

1.14.1 WATER POLLUTION

1.14.2 MAJOR ACCIDENT HAZARDS

1.14.3 AIR POLLUTION

1.15 ADDITIONAL REMARKS

1.16 LAST LITERATURE SEARCH

1.17 REVIEWS

1.18 LISTINGS E.G. CHEMICAL INVENTORIES

2.1 MELTING POINT

2.2 BOILING POINT

Value	:	224 deg. C.
Decomposition	:	
Method		other
Year	:	1982
GLP	:	no data
Test substance	:	other TS
Result	:	
Test substance	:	97 Adipate technical grade with purity of 99%.
Reliability	:	(2) valid with restrictions Solutia in-house study
Flag	:	Critical study for SIDS endpoint

18.11.2002 (3)

2.3 DENSITY

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Value	:	13 hPa at 224° C
Decomposition	:	
Method		other (measured)
Year	:	1982
GLP	:	no data
Test substance	:	other TS
Result	:	Other values: 4.4 hPa @ 200 degrees C; 36 hPA @ 250 degrees C.
Test substance	:	97 Adipate technical grade with purity of 99%.
Reliability	:	(2) valid with restrictions Data consistent with other values measured at temperatures above and below the temp. used in this study
Flag	:	Critical study for SIDS endpoint

18.11.2002 (3)

2.5 PARTITION COEFFICIENT

Log pow	:	> 6.48 at ° C
Method		other (measured)
Year	:	1980
GLP	:	no data
Test substance	:	other TS
Method	:	Used purified octanol (extracted 2X with H2SO4 and NaOH) and twice distilled deionized water. Four concentrations (110, 150, 1100 and 1200 ppm) of 97 Adipate in octanol were evaluated. The amount of 97 Adipate remaining in the octanol was determined by diluting the octanol with isooctane containing methyl stearate internal standard followed by GC/MS analysis. Level of detection was 5 ppb.
Result	:	After centrifuging the water to completely separate the phases, the average

concentration in all the waters was less than the lowest level of detection (< 5 ppb). Using this level a calculated lower limit for P was determined as >2.2 X 10E5 and a corresponding BCF calculated to be > 1000 using the method of Neely et al 1974. Environ Sci Technol 8:1113.

Test substance : Technical grade 97 Adipate is 99%.
Reliability : (2) valid with restrictions
Method consistent with OECD guidance and well documented.
Flag : Critical study for SIDS endpoint
18.11.2002 (11)

2.6.1 WATER SOLUBILITY

Value : < .048 mg/l at 25 ° C
Qualitative :
Pka : at 25 ° C
PH : at and ° C
Method : other
Year : 1982
GLP : yes
Test substance : other TS
Method : Saturator column technique used. A level of 5% 97 Adipate was coated on a 100 mesh Chromosorb WHP column, then loaded into a saturator column. Vials of eluent were collected, each containing isooctane with methyl stearate as an internal standard. Four vials were taken during a flow rate of 5 ml/m and 4 at a flow rate of 2.5 ml/m. 97 Adipate was measured by GC/MS using a level of 48 ppb as the limit of detection.
Result : A total of 8 samples were taken and analyzed, with no detectable 97 Adipate found in any sample. Hence, the water solubility was considered less than 48 ppb, the limit of detection in this assay.
Test substance : Technical grade is 99% pure.
Reliability : (2) valid with restrictions
Method consistent with OECD guidance and well documented.
Flag : Critical study for SIDS endpoint
24.10.2002 (13)

2.6.2 SURFACE TENSION

2.7 FLASH POINT

2.8 AUTO FLAMMABILITY

2.9 FLAMMABILITY

2.10 EXPLOSIVE PROPERTIES

2.11 OXIDIZING PROPERTIES

2.12 ADDITIONAL REMARKS

3.1.1 PHOTODEGRADATION

Type	:	water
Light source	:	Sun light
Light spect.	:	nm
Rel. intensity	:	based on Intensity of Sunlight
Direct photolysis		
Halflife t1/2	:	
Degradation	:	0 % after 14 day
Quantum yield	:	
Deg. Product	:	
Method	:	other (measured)
Year	:	1981
GLP	:	yes
Test substance	:	other TS
Method	:	Used sunlight photolysis screening method following ASTM E47.06 guidance, whereby 97 Adipate was added to quartz tubes containing either purified water or membrane-filtered river water and held either in darkness or in a combination of sunlight (14 hr) and darkness (10 hr), 24 hr/day for up to 14 days. A 0.107 g/100 ml 97 Adipate stock solution was made in acetonitrile; then 100 ul of a 10:100 ml dilution was injected into quartz tubes containing 10 ml of either membrane-filtered, purified water or membrane-filtered river water. A total of 20 tubes were prepared, with 4 tubes analyzed at time 0, and two tubes containing each type of water with test material that were analyzed after 2, 5, 9 and 14 days of testing. The ave. low temp. during this study was 64 degrees F. and the high ave. was 81 degrees F. Each test vial was extracted with isooctane and analyzed for test material by GC/MS. Due to initial results obtained, a stability experiment was also conducted in a similar pattern as before, except triplicate tubes were extracted immediately after spiking, after refrigeration and after sterilization with formaldehyde.
Result	:	Initial studies indicated rapid loss in both samples, those exposed to sunlight as well as those exposed to complete darkness; the T1/2 of samples exposed to darkness were equal to or less than those exposed to sunlight. These data suggested that phenomenon other than direct photolysis or chemical transformation was occurring. For this reason the stability study was conducted. Results of the stability study confirmed that no detectable photolytic or chemical transformation occurs after the addition of 97 Adipate and the loss observed in the initial studies were the result of biodegradation from contamination of bacteria in the test system.
Test substance	:	Technical grade is 99% pure.
Reliability	:	(2) valid with restrictions In-house study with good documentation.
Flag	:	Critical study for SIDS endpoint

24.10.2002 (12)

3.1.2 STABILITY IN WATER

Deg. Product	:	
Method	:	other (calculated)
Year	:	2002
GLP	:	no
Test substance	:	no data
Method	:	Calculated estimates from HYDROWIN, ver. 1.67.
Result	:	Half-life estimated to be 3.215 yr. Hydrolysis is slow at neutral pH and breaks down to mono ester and free alcohol.
Reliability	:	(2) valid with restrictions

Model used to estimate hydrolysis is recommended by US EPA for this purpose.

Flag : Critical study for SIDS endpoint
24.10.2002 (1)

3.1.3 STABILITY IN SOIL

3.2 MONITORING DATA

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type : fugacity model level III
Media :
Air (level I) : .278
Water (level I) : 3.61
Soil (level I) : 27.3
Biota (level II / III) :
Soil (level II / III) : 68.8
Method : other
Year : 2002
Method : Calculated using estimated values according to Mackay, Level III. Assumed emissions (1000 kg/hr) to air, water and soil compartments using following data inputs: Henry's LC=1.81e-005 atm-m3/mole (Henrywin program), Vapor Press=6.67e-005 mm Hg (Mpbpwin program), Liquid VP=7.46e-005 mm Hg (super-cooled), Melting Pt=29.9 deg C (Kowwin program) and Soil Koc=1.45e+007 (calc by model). Last soil entry included data estimate for sediments.

Results

```
Level III Fugacity Model (Full-Output):
=======================================
  Chem Name   : Hexanedioic acid, di-C7-9-branched and linear
alkyl esters
  Molecular Wt: 356.55
  Henry's LC  : 1.81e-005 atm-m3/mole (Henrywin program)
  Vapor Press : 6.67e-005 mm Hg  (Mpbpwin program)
  Liquid VP   : 7.46e-005 mm Hg  (super-cooled)
  Melting Pt  : 29.9 deg C (Mpbpwin program)
  Log Kow     : 7.55  (Kowwin program)
  Soil Koc    : 1.45e+007  (calc by model)

          Concentration   Half-Life    Emissions
            (percent)        (hr)       (kg/hr)
   Air        0.278          10.8         1000
   Water      3.61           900          1000
   Soil       27.3           900          1000
   Sediment   68.8           3.6e+003     0

              Fugacity    Reaction    Advection   Reaction
Advection
               (atm)      (kg/hr)      (kg/hr)    (percent)
(percent)
   Air       9.01e-012    855         133          28.5
4.44
   Water     1.78e-012    133         173          4.43
5.76
   Soil      1.06e-014    1.01e+003   0            33.5
0
   Sediment  1.20e-012    634         65.9         21.1
2.2

   Persistence Time: 1.6e+003 hr
   Reaction Time:    1.82e+003 hr
```

```
Advection Time:   1.29e+004 hr
Percent Reacted:  87.6
Percent Advected: 12.4

Half-Lives (hr), (based upon Biowin (Ultimate)and Aopwin):
   Air:      10.78
   Water:    900
   Soil:     900
   Sediment: 3600
     Biowin estimate: 2.692  (weeks-months)

Advection Times (hr):
   Air:      100
   Water:    1000
   Sediment: 5e+004
```

Reliability : (2) valid with restrictions
Estimated values based on model recommended by US EPA.
Flag : Critical study for SIDS endpoint
24.10.2002 (1)

3.3.2 DISTRIBUTION

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Type : aerobic
Inoculum :
Contact time :
Degradation : 67 - 88 % after 24 hour(s)
Result : readily biodegradable
Deg. Product :
Method : OECD Guide-line 302 A "Inherent Biodegradability: Modified SCAS Test"
Year : 1976
GLP : no
Test substance : other TS
Method : Two different measures of biodegradability were determined; 1) primary biodegradability measuring the disappearance of the analytical response for the original material was determined using the Semi-Continuous Activated Sludge (SCAS) technique, and 2) ultimate biodegradability, or conversion of the material to carbon dioxide, water, inorganic salts and normal metabolic products, was determined by carbon dioxide evolution procedures. The SCAS methodology followed that reported in J. Am Oil Chem Soc 46:432-440, a methodology consistent, but a predecessor of OECD test guideline 302. Test material was added to activated sludge obtained from a local domestic sewage treatment plant in 1.5 L glass vessels which were stirred magnetically at a level of 5 and 20 mg/24 hr. After a 3 week acclimation period, primary degradation was determined each week by analyzing 50-ml liquor samples withdrawn after feeding and at the end of the aeration cycle. Analysis was made using a GC with a FID detector. A blank unit was maintained on synthetic sewage without the addition of any test material. The Carbon dioxide Evolution test followed the procedures as outlined by Sturm (J. AM Oil Chem. Soc. 50:159-167, using both a T-D-S and Shake Flask system. The inoculum was prepared from a 14-day die away test.
Result : Primary biodegradation was determined to be 67+/- 14 % at the charge rate of 5 mg/24 hr of 97 Adipate and 88+/-5% at a rate of 20 mg/24 hr. ; CO2 evolution in the Ultimate biodegradation study was 90.2% and 78.7-

CO2 evolution in the Ultimate biodegradation study was 90.2% and 78.7-82.1% in the T-D-S and Shake flask methods tested, respectively.

Test substance : Technical grade 97 Adipate with purity of 99%.

Conclusion : Rapid and essentially complete degradation was observed in both the SCAS and CO2 Evolution tests, indicating rapid degradation by microbial populations in the environment.

Reliability : (1) valid without restriction
OECD Methodology, well documented.

Flag : Critical study for SIDS endpoint

18.11.2002 (2)

3.6 BOD5, COD OR BOD5/COD RATIO

3.7 BIOACCUMULATION

3.8 ADDITIONAL REMARKS

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	static
Species	:	Oncorhynchus mykiss (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
Analytical monitoring	:	no
NOEC	:	> 1000
LC0	:	> 1000
Method	:	other
Year	:	1980
GLP	:	yes
Test substance	:	other TS
Method	:	Followed methods described in EPA-600/3-75-009, Methods for Acute Toxicity tests with Fish, Macroinvertebrates and Amphibians, 1975. The test treatments were prepared by individually mixing the appropriate amount of test substance with 10 ml of actone and adding it directly to the test chambers. The control also received 10 ml of acetone. One replicate was prepared for each test treatment and control. The test was performed in 5-gallon glass vessels containing 15 L of dilution water. The dilution water was filtered well-water. each treatment vessel contained 10 fish. Fish were obtained from Fenders' Fish Hatchery in Baltic, Ohio and had a mean lenth of 33 mm and weight of 0.43 g. Well water hardness was 225 ppm CaCo3.
Result	:	No mortalities were observed in any of the test concentrations tested, including: control, 100, 180, 320, 560 or 1000 mg/L. thus the LC50 is considered to be > 1000 mg/L. It should be recognized that the test substance was insoluble at all test levels as an oily sheen was seen in each treated vessel. Test temp. was 12+/-1 Deg C.; the pH range was 7.7-7.9 and Dissolved oxygen ranged from 8.6 -10 mg/L.
Test substance	:	Technical grade with purity of 99%.
Reliability	:	(2) valid with restrictions Study conducted according to well accepted test guidelines which preceeded OECD guidance and was well documented. Established that level of toxicity was above solubility limit (48ppb) of this test agent, although value cited for LC50 is far in excess.
Flag	:	Critical study for SIDS endpoint

09.10.2002 (5)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type	:	static
Species	:	Daphnia magna (Crustacea)
Exposure period	:	48 hour(s)
Unit	:	mg/l
Analytical monitoring	:	no
EC50	:	= 1.9
Method	:	other
Year	:	1980
GLP	:	yes
Test substance	:	other TS
Method	:	Followed methods outlined in USEPA, 660/3 -75-009. Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians. 1975. Test treatments were prepared by adding the test substance with 0.2 ml acetone directly to the test treatments. Two replicates of 10 organisms were tested per treatment. Test vessels were 250 ml beakers with 200 ml of test solution. The dilution water was well water. A moving average angle, Probit or Bionomial method was used for statistical analysis.

or Bionomial method was used for statistical analysis.

Result : An LC50 of 1.9 mg/L with CI of 1.5-2.3 mg/L. Mortality (%) observed at following levels: Control (0%), solvent control (0%), 1 mg/L (0%), 1.8 mg/L (55%), 3.2 mg/L (95%), 5.6 mg/L (85%), 10 mg/L (100%), 18 mg/L (100%). Test substance was observed on the surface of all treatment test vessels. Daphnids were observed trapped in the test substance, which affected immobilization.Test temp. was 20 +/-1 Deg. C., the pH was 7.4 during the study and the Dissolved oxygen was 9.2 mg/L. Water hardness was reported as 225 ppn CaCO3. Daphnia were < 24 hr old and obtained from in-house stock. Lighting was 16 hrs light and 8 hrs dark.

Test substance : Technical grade material with purity of 99%..

Conclusion : LC50 value above the level of solubility (i.e. < 1mg/L) is unreliable in this test due to test material interference and immobilization of test organisms above 1 mg/L. However, at a test level slightly above the determined level of solubility (1 mg/L) no deaths occurred and thus no interference with test material affected test results. Thus, this study is adequate to judge the lack of toxicity of this test agent at the level of water solubility.

Reliability : (2) valid with restrictions This study provides adequate information at the level of water solubility, where no toxicity was observed, in a well documented study conducted according to EPA test guidelines established prior to OECD codification of similar guidance.

Flag : Critical study for SIDS endpoint

09.10.2002 (6)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species : Selenastrum capricornutum (Algae)

Endpoint : growth rate

Exposure period : 96 hour(s)

Unit : mg/l

Analytical monitoring : no

EC50 : = 2.5

Method : other

Year : 1980

GLP : yes

Test substance : other TS

Method : Followed US EPA Printz Algal Assay Test (1978). A primary stock was prepared by adding the test substance to dimethylformamide (DMF). Secondary stock solutions (test treatments) were then prepared by serial dilution using the primary stock. A solvent control (0.05 ml, max. amount added to any test flask) of DMF was also tested. Algal growth medium was used as the control. Three replicates of each test treatment were tested. The initial algal concentration was 2.0X10E4 cells per ml.Lighting was = 4000 lux; temp. was 24+/-1 Deg. C; the pH range was 7.1-7.2. Algal culture stock was obtained from USEPA Environmental Research Laboratory, Corvallis, Oregon. Statistical methods used: probit, linear regression, Student's t-test for growth differences.Chlorophyll was measured daily using a Turner filter fluorometer. Cell counts were performed via a hemacytometer at study termination.

Result : EC50 (based on cell nos.) = 2.5 ppm; EC50 (based on chlorophyll measurements) = 1.8 ppm; Differences (between test level and control level) seen at 96 h in Chlorophyll: solvent control (0%), 0.3 mg/L (+17%), 0.6 mg/L (-13%), 1.2 mg/L (-56%), 2.5 mg/L (-61%), and 5 mg/L (-70%). Differences in cell no. at similar levels were: solvent control (-1%), 0.3 mg/L (+4%), 0.6 mg/L (-7%), 1.2 mg/L (-47%), 2.5 mg/L (-54%), and 5 mg/L (-62%).

Test substance : Technical grade test material was 99% pure.

Reliability : (2) valid with restrictions
Provides adequate toxicity information (NOEL < 48 ppb) up to the level of solubility, although EC50 is reportedly higher than the solubility limit.

Flag : Critical study for SIDS endpoint
27.09.2002 (8)

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

4.5.1 CHRONIC TOXICITY TO FISH

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

4.6.1 TOXICITY TO SOIL DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

4.6.3 TOXICITY TO OTHER NON-MAMM. TERRESTRIAL SPECIES

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

5.1.1 ACUTE ORAL TOXICITY

Type	:	LD50
Species	:	rat
Strain	:	Sprague-Dawley
Sex	:	male/female
Number of animals	:	10
Vehicle	:	other
Value	:	> 15800 mg/kg bw
Method	:	other
Year	:	1970
GLP	:	no
Test substance	:	other TS
Method	:	Undiluted test material was fed by stomach tube to rats in increasing doses at increments of fractional log intervals. The dose levels were 2000, 3160, 5010, 7940, 12600 and 15800 mg/kg. Single rats were used for the lower doses while 5 rats (3 male, 2 female) were used at 15800 mg/kg. Daily observations were made for toxic signs and a complete necopsy was performed after 7 days.
Result	:	No animals died at any dose level. Toxic signs reported as reduced appetite and activity for 1-4 days and slight weakness. All rats were considered normal after 7 days. At necropsy, 2/5 rats at 15800 mg/kg were observed with slight congestion of the lungs.
Test substance	:	>99% pure
Conclusion	:	Compound considered practically non-toxic by oral ingestion in male and female rats.
Reliability	:	(2) valid with restrictions Conducted pre-GLP, but adequately documented.
Flag	:	Critical study for SIDS endpoint

03.09.2002 (14)

5.1.2 ACUTE INHALATION TOXICITY

5.1.3 ACUTE DERMAL TOXICITY

Type	:	LD0
Species	:	rabbit
Strain	:	New Zealand white
Sex	:	male/female
Number of animals	:	5
Vehicle	:	other
Value	:	> 7940 mg/kg bw
Method	:	other
Year	:	1970
GLP	:	no
Test substance	:	other TS
Method	:	Undiluted compound was applied in increasing doses at increments of 0.2 fractional log intervals to closely clipped, intact skin of male and female rabbits. Single animals were tested at lower dosages while 1 male and 1 female rabbit were tested at the highest level. The dose levels were 2000, 3160, 5010 and 7940 mg/kg. Treated areas were covered with plastic strips (occluded) and animals held in wooden stocks for 24 hrs before removal. Animals were observed for signs of toxicity for 14 days, after which they were necropsied and evaluated for macroscopic lesions.
Result	:	No deaths were observed in the study. Toxic signs reported were reduced appetite and activity, slight lethargy (2-5 days duration) and slight tremors (1-2 days) at 5010 and 7940 mg/kg. At necropsy, rabbits at 5010 and

(1-2 days) at 5010 and 7940 mg/kg. At necropsy, rabbits at 5010 and 7940 mg/kg were observed with slight congestion of the lungs and areas of slight discoloration of the liver.

Test substance	:	> 99% pure
Conclusion	:	Compound was considered practically non-toxic by dermal exposure in male and female rabbits.
Reliability	:	(2) valid with restrictions Pre-GLP study; provided as Supplemental information.

18.11.2002 (14)

5.1.4 ACUTE TOXICITY, OTHER ROUTES

5.2.1 SKIN IRRITATION

5.2.2 EYE IRRITATION

5.3 SENSITIZATION

5.4 REPEATED DOSE TOXICITY

Species	:	rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	oral feed
Exposure period	:	90 days
Frequency of treatment	:	Daily
Post obs. period	:	None
Doses	:	0 (negative control), 0.1, 0.5 and 2.5 %;
Control group	:	yes, concurrent no treatment
NOAEL	:	> 2.5 %
Method	:	other
Year	:	1972
GLP	:	no
Test substance	:	other TS
Method	:	Methodology consistent with OECD 408 but preceeded codification. Groups of 15 male and 15 female rats were administered diets containing test substance at 0, 0.1, 0.5 or 2.5% for 13 weeks. The high dose male rats received approx. 1300 mg/kg/d and females received 1800 mg/kg/d. A comparative group of 15 rats/sex were given 2.5% dioctyl adipate. Body weights (15/sex/group) and food consumption (5/sex/group) were measured weekly. Individual animal observations were recorded daily and detailed exams performed weekly. No ophthalmoscopic exam was performed. Hematology (Hgb, Hct, RBC, Total and differential leukocytes), clinical blood chemistry (SAP, BUN, SGPT, fasting blood glucose) and urine analysis (Glu, Alb, pH, specific gravity, microscopic elements) were performed on 10 rats/sex/group from the untreated control group, the high dose test group and the DOA test group after 45 and 84 days on test. Absolute and relative organ weights were recorded for liver, kidney, spleen, gonads, heart and brain at study term ination. After 90 days, each rat was necropsied. A complete set of approx. 40 tissues was examined from 10 rats/sex from the untreated control group, the high dose test group, and the DOA group. Mean body weight, food consumption and organ weight values were evaluated by analysis of variance (ANOVA) and significant differences among the groups were examined by t-test. A level of $p<0.05$

differences among the groups were examined by t-test. A level of p<0.05 was used to determine significance.

Result : Three deaths occurred during the study and were attributed to an acute respiratory infection. There were no differences noted between the untreated control and any of the Di (C7-C9 alkyl) adipate test groups for body weights, food consumption, or blood or urine parameters. Small but significantly Increased absolute and relative kidney weights were noted for females, but not males, in the high dose group. These findings were not considered treatment-related based on the small changes seen only in females without corresponding clinical or microscopic parameters which would be indicative of a renal effect. Necropsy findings were considered spontaneous and not test substance-related. The most frequent findings in all groups were lesions in the trachea and lungs consistent with chronic infection. No weight changes nor microscopic findings indicative of a treat-related effect were observed in gonads from either sex. Dioctyl adipate (DOA) exhibited statistically significantly decreased body weight gains (both sexes) and statistically increased female kidney and liver weights and weight ratios.

Test substance : > 99% pure

Reliability : (2) valid with restrictions
Study underwent independent audit and judged to have met Acceptable standard by FDA. Individual data not presented in report.

Flag : Critical study for SIDS endpoint

18.11.2002 (9)

5.5 GENETIC TOXICITY 'IN VITRO'

Type : Ames test

System of testing : S. typhimurium strains TA98, TA100, TA1535 and TA1537

Concentration : 0.0, 0.01, 0.04, 0.2, 1.0, 3.0, and 10.0 uL/plate and 25 uL/spot in spot test

Cycotoxic conc. : none observed at highest dose tested of 10 uL/plate in plate incorporation assay

Metabolic activation : with and without

Result : negative

Method : OECD Guide-line 471 "Genetic Toxicology: Salmonella thyphimurium Reverse Mutation Assay"

Year : 1981

GLP : yes

Test substance : other TS

Method : Positive control chemicals were sodium nitrite, benzo(a)pyrene, 2-nitrofluorene, 9-aminoacridine and 2-aminoanthracene; the solvent control was ethanol. Concurrent solvent and positive controls were included in all experiments and performed as expected. A toxicity pretest with TA 100 was conducted with and without microsomal activation to determine cytotoxicity and identify the highest dose level to be used in the full study. Both plate incorporation and spot tests were conducted in triplicate in all strains with and without activation. A mutagenic response was defined as a reproducible, dose-related increase in the number of histidine-independent colonies over the spontaneous incidence. Bartlett's test was run to determine whether significant differences existed among treatment variables. Treatment groups were compared to solvent control using a 1-sided t-test and within level pooled variance. Dose response was further evaluated for all treatment groups found to be significantly (p<0.01) higher than solvent control.

Result : The substance was not mutagenic at doses up to 10 uL/plate in Salmonella strains TA 98, TA 100, TA 1535 and TA 1537 in the plate incorporation assay nor at 25 uL/spot in the spot test with or without metabolic activation. No microbial toxicity was observed in strain TA100 at concentrations up to 10 uL/plate in plate incorporation assay nor at 25 uL/spot in the spot test with or without metabolic activation. Decreased solubility was observed at 3

and 10 uL in the plate incorporation assay.

Test substance	:	> 99% pure
Conclusion	:	The test substance was not mutagenic in all strains tested.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

03.09.2002 (10)

5.6 GENETIC TOXICITY 'IN VITRO'

5.7 CARCINOGENITY

5.8 TOXICITY TO REPRODUCTION

5.9 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species	:	rat
Sex	:	female
Strain	:	Sprague-Dawley
Route of admin.	:	gavage
Exposure period	:	Gestation days 6-19
Frequency of treatment	:	Daily during the gestation period
Duration of test	:	Animals were sacrificed on gestation day 20
Doses	:	0, 1000, 4000 and 7000 mg/kg/d
Control group	:	yes, concurrent vehicle
NOAEL Maternalt.	:	>= 4000 mg/kg bw
NOAEL Teratogen	:	>= 7000 mg/kg bw
NOAEL Embryotoxicity	:	>= 4000 mg/kg bw
NOAEL Fetotoxicity	:	>= 4000 - mg/kg bw
Method	:	OECD Guide-line 414 "Teratogenicity"
Year	:	1981
GLP	:	yes
Test substance	:	other TS
Method	:	Females were cohabited overnight with males in a 2:1 ratio. Gestation day 0 was determined the morning that vaginal sperm or plug was found. Mated females were assigned to groups to achieve 24/group. Female rats were dosed daily on Days 6-19 of gestation. Body weights were recorded on GD 0, 6, 15 and 20. Individual clinical observations were recorded on GD 0, 6, 10, 15 and 20. Animals were sacrificed on GD 20 and intact uteri were removed and weighed. All fetuses were weighed and examined for external abnormalities; approximately one half were processed for skeletal examination and one half preserved for soft tissue examination. Mean data was analyzed using analysis of variance (ANOVA). Bartlett's test was used to test for equal variance and Dunnett's test for differences from control For incidence data, a Chi-square analysis and Fisher's Exact Probability test were used, followed by Armitage's test for linear trend, if needed.
Result	:	No dams died during the study. Significant maternal body weight decreases ($p<0.01$) were observed at 7000 mg/kg/d. There were no significant differences in the number of implantations, live fetuses, resorptions or corpea lutea. There were no statistically significant effects on mean fetal body weight or sex ratio. High dose (7000 mg/kg) male and female fetal weights were slightly, but not statistically, reduced from the control, low and mid dose groups. There were no differences among groups for fetal ossification variations, external, visceral or skeletal malformations. A higher incidence of rudimentary structures was observed in high dose fetuses when compared to controls, but were within the range

in high dose fetuses when compared to controls, but were within the range of historical controls at this laboratory.

Test substance : > 99% pure
Conclusion : No evidence of developmental toxicity was observed at dose levels of 1000 and 4000 mg/kg/day. Maternal toxicity (reduced body weight) and embryotoxicity (reduced fetal weight) was observed at the highest dose (7000 mg/kd/d) tested.
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
27.09.2002 (7)

5.10 OTHER RELEVANT INFORMATION

5.11 EXPERIENCE WITH HUMAN EXPOSURE

(1) EPIWIN, version 3.10. 2002. Syracuse Research Corp., Syracuse, NY.

(2) Saeger, VW, RG Kaley II, O Hicks, ES Tucker and JP Mieure. 1976. Appl Environ Microbiol. 31 (5):746-749.

(3) Solutia in-house study and cited on MSDS, 2002

(5) Solutia Study no. AB19800352. Acute toxicity of S-97A to Rainbow Trout.

(6) Solutia Study no. AB19800354. Acute toxicity of Santicizer 97A to Daphnia magna.

(7) Solutia Study no. BD-81-131. Teratogenicity study in rats with Santicizer 97.

(8) Solutia Study no. BN19800355. Toxicity of Santicizer 97A to the freshwater algae Selenstrum capricornatum.

(9) Solutia study no. BT-71-38. 90-Day subacute oral toxicity study with Santicizer 97 in albino rats.

(10) Solutia Study no. DA-80-503.Salmonella Mutagenicity Assay of Santicizer 97.

(11) Solutia study no. ES-80-SS-41. Octanol/Water Partition Coefficient of SANTICIZER 97A and Dioctyl Adipate.

(12) Solutia Study no. MO19820071.Sunlight photolysis screening of Santicizer 97.

(13) Solutia study no. MO20020442. Aqueous solubility of Santicizer 97.

(14) Solutia Study no. Y-70-112; Acute Toxicological Investigation of Santicizer 97A [EPA Document no. 88-920007905]

7.1 END POINT SUMMARY

7.2 HAZARD SUMMARY

7.3 RISK ASSESSMENT